

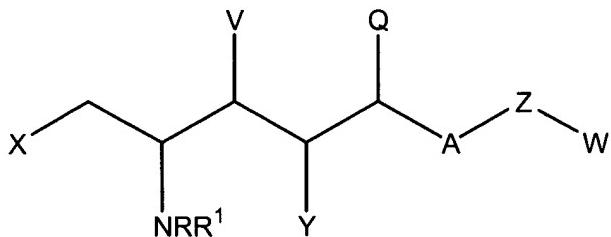
Appl. No. : 10/647,801
Amendment dated September 13, 2004
Responsive to Office Action dated August 11, 2004

Amendment to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (Currently Amended) A method for the treatment of an abnormal cell proliferative disorder comprising administering an effective treatment amount of a sphingolipid derivative of the formula:



wherein

A is a spacer group which is $(CH_2)_m$ where $m=0-14$, where any of the hydrogens may be independently replaced by R¹ or X and where any two adjacent carbons may be independently replaced by a C₃-C₈ cycloalkyl group, a 1,2-, 1,3-, or 1,4-disubstituted benzene group, or a 2,3-, 2,4- or 2,5-disubstituted thiophene, furan or pyrrole group;

X, Y, V, and Q are independently hydrogen, OR¹, NR₂, CN, alkyl, acyl[[,]] or carboxylate, and wherein alternatively, V and Y or Y and Q or Q and A can together constitute a double or triple bond;

X is hydrogen

W = no substituent, H, alkyl, aryl, alkenyl, alkynyl, alkaryl, aralkyl, C(O)(CH₂)_nCO₂H, C(O)(CH₂)_nCW'CO₂H, or OR¹ ;

W' is selected independently from H, alkyl, aryl, (CH₂)_nCO₂H; (CH₂)_nCH(CO₂H)CH₂CO₂H; and (CH₂)_nCH(CO₂H)CH(CH₂CO₂H)CO₂H;

Z is H, O, NH, NR, NHC(O), CO₂, C(O)NH, or C(O)NR;

R is selected independently from H, alkyl, acyl, alkenyl, alkynyl, aryl, alkaryl, aralkyl, or heteroaryl;

R¹ is R or R²;

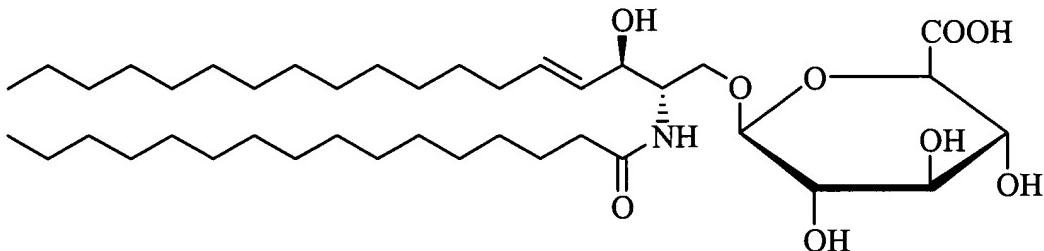
R² is phosphate (OP(OR₃), wherein at least one R is not hydrogen), [[b]]β-D-galactoside, N-acetyl-[[b]]β-D-glucosamine, [[a]]α-D-mannoside, ~~an organic azo bond containing moiety that can be reduced by an azoreductase~~, [[b]]β-D-cellulosides, [[b]]β-D-glucopyranosides, [[b]]β-D-galactopyranosides, [[b]]β-D-glucuronides, starch, lactose, raffinose, stachyose, fructooligosaccharides fructo-oligosaccharide or, ~~an amide or ester of [[b]]β-cyclodextrin, or dextran linked via succinate and glutarate, or an amino acid or peptide, or a polyamino acid or polypeptide, furanose or and pyranose carbohydrates, sulfonate (and esters thereof), phosphocholine, phosphoserine, and phosphoethanolamine;~~

wherein there is at least one R² substituent in the sphingolipid derivative, optionally in a pharmaceutically acceptable carrier to a host in need thereof.

2. (Canceled).

3. (Currently Amended) [[A]] The method compound of claim 1, wherein R² is selected from the group consisting of ceramide β-glucuronide; sphinganine β-glucuronide; dihydroceramide β-glucuronide; sphingomyelin β-glucuronide; sphingosine β-glucuronide; ceramide [[b]]β-D-galactoside; sphinganine b-D-galactoside dihydroceramide b-D-galactoside; sphingomyelin b-D-galactoside; sphingosine b-D-galactoside; ceramide N-acetyl-[[b]]β-D-glucosamine; sphinganine N-acetyl b-D-glucosamine; dihydroceramide N-acetyl b-D-glucosamine; sphingomyelin N-acetyl b-D-glucosamine; sphingosine N-acetyl b-D-glucosamine; ceramide [[a]]α-D-mannoside; sphinganine α-D-mannoside; dihydroceramide α-D-mannoside; sphingomyelin α-D-mannoside; sphingosine α-D-mannoside; ceramide [[b]]β-D-celluloside; sphinganine b-D-celluloside; dihydroceramide b-D-celluloside; sphingomyelin b-D-celluloside; ceramide and [[b]]β-D-glucopyranoside; sphinganine b-D-glucopyranoside; dihydroceramide [b]β-D-glucopyranoside; sphingomyelin b-D-glucopyranoside; sphingosine b-D-glucopyranoside; ceramide b-D-galactopyranoside; sphinganine b-D-galactopyranoside; dihydroceramide b-D-galactopyranoside; sphingomyelin b-D-galactopyranoside; and sphingosine b-D-galactopyranoside.

4. (Currently Amended) A method for the treatment of an abnormal cell proliferative disorder comprising administering an effective treatment amount of a Ceramide β-glucuronide, which has the chemical formula



optionally in a pharmaceutically acceptable carrier to a host in need thereof.

5. (Currently Amended) The compound The method of claims claim 1 or 2, wherein the bond between V and Y,orY and Q orQ and A is double bond.

6.-9 (Canceled)

10. (Currently Amended) A The method of any one of claims 1 or 3-5 wherein the proliferative disorder is for the treatment of a benign or malignant tumor comprising administering an effective treatment amount of a compound of any one of claims 1-8 to a host in need thereof.

11. (Canceled)

12. (Currently Amended) The method of any one of claims 1 or 3-5 claim 9, wherein the proliferative disorder is selected from the group consisting of colon cancer, intestinal polyps, intestinal tumors, inflammatory bowel diseases, ulcerative colitis and Crohn's disease, necrotizing enterocolitis, ileocecalis, other inflammations of the lower bowel, antibiotic associated colitis, and tumors of the urogenital tract.

13. (Currently Amended) The method of any of claims 1 or 3-5 claim 9, wherein the disorder is colon cancer.

14. (Currently Amended) The method of any of claims 1 or 3-5 claim 9, wherein the disorder is a benign tumor is selected from the group consisting of papilloma, adenoma, firoma, chondroma, osteoma, lipoma, hemangioma, lymphangioma, leiomyoma, rhabdomyoma,

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meningioma, neuroma, ganglioneuroma, nevus, pheochromocytoma, neurilemona, fibroadenoma, teratoma, hydatidiform mole, granuosa-theca, Brenner tumor, arrhenoblastoma, hilar cell tumor, sex cord mesenchyme, interstitial cell tumor, and thyoma.

15. (Currently Amended) The method of claim 10, wherein the tumor is selected from the group consisting of a malignant tumors tumor (cancer), prostatic adenocarcinoma, bladder carcinoma, ~~and~~ adenocarcinoma, fibrosarcoma, chondrosarcoma, osteosarcoma, liposarcoma, hemangiosarcoma, lymphangiosarcoma, leiomyosarcoma, rhabdomyosarcoma, myelocytic leukemia, erythroleukemia, multiple myeloma, glioma, meningeal sarcoma, thyoma, cystosarcoma phyllodes, nephroblastoma, teratoma choriocarcinoma, cutaneous T-cell lymphoma (CTCL), cutaneous tumors primary to the skin, breast and other tumors infiltrating the skin, Kaposi's sarcoma, and premalignant and malignant diseases of mucosal tissues.

16. (Currently Amended) The method of any of claims 1 or 3-5 claim 9, wherein the disorder is selected form the group consisting of preneoplastic lesions, mycosis fungoides, psoriasis, dermatomyositis, rheumatoid arthritis, viruses, molluscum contagiosum, premalignant and malignant diseases of the female genital tract.

17. (Canceled)

18. (Currently Amended) ~~A The method of claim 1 wherein the administration triggers for triggering the release of cytochrome c in a patient in need thereof comprising administering an effective treatment amount of a compound of any one of claims 1-8.~~

19. (Currently Amended) ~~A The method of claim 1 wherein the administration inhibits for inhibiting protein kinase c in a patient in need thereof, comprising administering an effective treatment amount of a compound of any one of claim 1-8.~~

20. (Currently Amended) ~~A The method of claim 1 wherein the administration promotes promoting cell differentiation in a patient in need thereof, comprising administering an effective treatment amount of a compound of any one of claims 1-8.~~

21. (Currently Amended) ~~The method of claim 10 further A method for treating a tumor in a patient comprising administering an effective treatment amount of a compound of claim 6 or 7 in combination with a chemotherapeutic agent.~~

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22. (Original) The method of claim 21, wherein the chemotherapeutic agent is doxorubicin.

23-28 (Canceled)

29. (New) The method of claim 1, wherein Y is hydrogen.
30. (New) The method of claim 1, wherein V is OR².
31. (New) The method of claim 30, wherein V is O-β-D-galactoside.
32. (New) The method of claim 30, wherein V is O-β-D-glucuronide.
33. (New) The method of claim 30, wherein V is O-(N-acetyl-β-D-glucosamine).
34. (New) The method of claim 30, wherein V is O-α-D-mannoside.
35. (New) The method of claim 30, wherein V is O-β-D-celllobioside.
36. (New) The method of claim 30, wherein V is O-β-D-glucopyranoside.
37. (New) The method of claim 30, wherein V is O-β-D-galactopyranoside.
38. (New) The method of claim 30, wherein V is O-β-D-galactopyranoside.
39. (New) The method of claim 1, wherein Y is H and V is OR².
40. (New) The method of claim 39, wherein V is O-β-D-galactoside.
41. (New) The method of claim 39, wherein V is O-β-D-glucuronide.
42. (New) The method of claim 39, wherein V is O-(N-acetyl-β-D-glucosamine).
43. (New) The method of claim 39, wherein V is O-α-D-mannoside.
44. (New) The method of claim 39, wherein V is O-β-D-celllobioside.
45. (New) The method of claim 39, wherein V is O-β-D-glucopyranoside.
46. (New) The method of claim 39, wherein V is O-β-D-galactopyranoside.
47. (New) The method of claim 39, wherein V is O-β-D-galactopyranoside.
48. (New) The method of claim 1, wherein Q is OR².

49. (New) The method of claim 48, wherein Q is O- β -D-galactoside.
50. (New) The method of claim 48, wherein Q is O- β -D-glucuronide.
51. (New) The method of claim 48, wherein Q is O-(N-acetyl- β -D-glucosamine).
52. (New) The method of claim 48, wherein Q is O- α -D-mannoside.
53. (New) The method of claim 48, wherein Q is O- β -D-cellobioside.
54. (New) The method of claim 48, wherein Q is O- β -D-glucopyranoside.
55. (New) The method of claim 48, wherein Q is O- β -D-galactopyranoside.
56. (New) The method of claim 48, wherein Q is O- β -D-galactopyranoside.
57. (New) The method of claim 1, wherein Y is H and Q is OR².
58. (New) The method of claim 57, wherein Q is O- β -D-galactoside.
59. (New) The method of claim 57, wherein Q is O- β -D-glucuronide.
60. (New) The method of claim 57, wherein Q is O-(N-acetyl- β -D-glucosamine).
61. (New) The method of claim 57, wherein Q is O- α -D-mannoside.
62. (New) The method of claim 57, wherein Q is O- β -D-cellobioside.
63. (New) The method of claim 57, wherein Q is O- β -D-glucopyranoside.
64. (New) The method of claim 57, wherein Q is O- β -D-galactopyranoside.
65. (New) The method of claim 57, wherein Q is O- β -D-galactopyranoside.
66. (New) The method of any of claim 10 wherein the disorder is a malignant tumor.
67. (New) The method of any of claim 10 wherein the disorder is a glioma.
68. (New) The method of any of claim 10 wherein the disorder is a myeloma.
69. (New) The method of any of claim 10 wherein the disorder is a papilloma.
70. (New) The method of any of claim 10 wherein the disorder is a carcinoma.
71. (New) The method of any of claim 10 wherein the disorder is a fibrosarcoma.